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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,854	11/14/2001	Avi J. Ashkenazi	P2730P1C24	3241

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EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,854	GENENTECH,INC.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Sequence Comparisons A-C.

DETAILED ACTION

1. Formal Matters

A. The Preliminary Amendment dated 11/14/01, has been entered into the record.

B. Claims 119-124 are pending and are the subject of this Office Action.

2. Priority

According to the priority statement of 9/3/02, it appears that the claimed subject matter defined in the instant application is supported by the parent application serial no. 60/097,661. However, the Examiner has concluded that the subject matter defined in this application is not supported by any of the applications in the chain of priority because the presently claimed subject matter is not supported by a specific, substantial or well-established utility, nor, for this reason, is it enabled. Accordingly, the subject matter defined in claims 119-124 has an effective filing date of 11/24/01, which is the filing date of the present application.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to 11/24/01 which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to 11/24/01.

3. Information Disclosure Statement

A. References A1 and A2 have been lined through since they are not in proper format, including author and date of deposit.

4. Specification

A. Though none could be found, due to the length of the specification, Applicants are reminded that embedded hyperlink and/or other form of browser-executable code are not permitted in the specification. See MPEP § 608.01.

B. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title recites polypeptides and polynucleotides whereas the claims are drawn to antibodies.

5. Claim Objections

A. The syntax of claims 119 and 124 could be improved by replacing the phrase "shown in Figure 228 (SEQ ID NO:314)" with "of SEQ ID NO:314."

6. Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A. Claims 119-124 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility. These claims are directed to antibodies which bind to the protein of SEQ ID NO:314. However, the invention encompassed by these claims has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines, published 1/5/01, 66 FR 1092. The instant application has provided a description of an isolated protein. However, the instant application does not disclose a specific and substantial biological role of this protein or its significance.

However, it is clear from the instant specification that the claimed antibody which binds to what is termed an "orphan receptor" in the art. The instant application does not disclose the biological role of the claimed protein or its significance. Applicants disclose in the specification that the receptor has certain amino acid sequence identity with microfibril-associated glycoprotein 4 (MFA4 HUMAN); ficolin-A - Mus musculus (M0078131); human lectin P35 (D63155561); ficolin B - Mus musculus (AF00632171); human tenascin-R (restriction) (HS518E13 1); the long form of a rat janusin precursor (A45445); fibrinogen-related protein HFREP-I precursor (JNO596); a human Tenascin precursor (TENA HUMAN); hllman CDT6 (HSY16132 1); and angiopoietin-l - Mus musculus (MM1.183509 1). Therefore, Applicants believe that NL7 disclosed the present application is a novel TIE ligand homologue, and may play a role in angiogenesis and/or vascular maintenance and/or wound healing and/or inflammation and/or tumor development and/or growth. However, homology alone is not sufficient to demonstrate utility of the present invention. There is little doubt that, after complete characterization, this protein will

probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicants' claimed invention is incomplete.

The instant situation is directly analogous to that of which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The specification discloses that the polynucleotides of the invention encode proteins which have significant sequence similarity to known proteins. Based on the structural similarity, the specification asserts that the newly disclosed SEQ ID NO:314 has similar activities. The assertion that the disclosed proteins have biological activities similar to known proteins cannot be accepted in the absence of supporting evidence, because generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases

in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene.

Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the protein of SEQ ID NO:314 which is only known to be homologous to various receptors. Therefore, the instant claims are drawn to a polynucleotide encoding a protein which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said protein identified in the specification. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for said protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Furthermore, since the protein of the invention is not supported by a specific and substantial asserted utility or a well established utility, the claimed antibodies also lack utility.

7. Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 119-124 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claim 122 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not understood how an antibody can be both an "antibody" and a "fragment." Applicants may want to consider amending the independent claim to recite, for example "an antibody, or fragment thereof, which binds..." and canceling claim 122.

B. Claim 124 is confusing since it is not clear what the definition of "specifically binds" is. This term is not defined in the specification. Furthermore, it is not clear how this claim differs from that of claim 119, where the antibody "binds" the protein of SEQ ID NO:314.

9. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 119-124 are rejected under 35 U.S.C. 102(b) as being anticipated by Baker et al. (WO 99/63088). The claims recite an antibody which binds to the protein of SEQ ID NO:314. The claims also

recite a monoclonal, polyclonal, humanized, or labeled antibody. Baker et al. teach a protein which is 100% identical to SEQ ID NO:314 of the present invention (Sequence Comparison A). Baker also teach monoclonal, polyclonal, humanized, labeled antibodies and antibody fragments (page 309, lines 16-21; page 311, line 28 – page 313, line 6 and page 365, line 16 – page 368, line 37).

B. Claims 119-124 are rejected under 35 U.S.C. 102(b) as being anticipated by Fernandez et al. (WO 00/61754). The claims recite an antibody which binds to the protein of SEQ ID NO:314. The claims also recite a monoclonal, polyclonal, humanized, or labeled antibody. Fernandez et al. teach a protein which is 100% identical to 269 contiguous amino acids of SEQ ID NO:314 of the present invention (Sequence Comparison B). Fernandez also teach monoclonal, polyclonal, humanized and labeled antibodies as well as fragments thereof (pages 36-39, especially page 36, line 13; page 37, lines 8 and 19; page 38, line 9 and page 39, line 6).

C. Claims 119-124 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhao et al. (Hum. Mol. Genetics). The claims recite an antibody which binds to the protein of SEQ ID NO:314. The claims also recite a monoclonal, polyclonal, humanized, or labeled antibody. Zhao et al. teach a protein which is 100% identical to 8 contiguous amino acids of SEQ ID NO:314 of the present invention (Sequence Comparison C). Zhao teach antibodies which bind this protein (top left column of page 592). These antibodies were used in a Western Blot. Therefore, the artisan would immediately envision a labeled polyclonal antibody.

10. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 119-124 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al. in view of Fernandez. The teachings of Zhao and Fernandez are seen in the above rejection under 35 USC 102. Zhao do not specifically teach monoclonal or humanized. However, Fernandez do teach these antibodies. It would have been obvious for one of ordinary skill in the art at the time of the present

invention to have made monoclonal, labeled or humanized antibodies in view of the teachings of Fernandez (pages 36-39). The artisan would have been motivated to make these antibodies in order to produce an antibody to a specific epitope of the protein of Zhao (monoclonal), or for detecting the protein (labeling) or any type of use involving humans, or the human variants of the protein of Zhao (humanized.)

11. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
February 27, 2004

ROBERT LANDSMAN
PATENT EXAMINER

Sequence Comparison A

```
ID   AAY66727 standard; protein; 461 AA.
XX
DT   05-APR-2000  (first entry)
XX
DE   Membrane-bound protein PRO1346.
XX
KW   Membrane-bound polypeptide; PRO polypeptide; LDL receptor; TIE ligand;
KW   pharmaceutical; receptor immunoadhesin; gene mapping.
XX
OS   Homo sapiens.
XX
PN   WO9963088-A2.
XX
PD   09-DEC-1999.
XX
PF   02-JUN-1999;   99WO-US12252.
XX
PR   02-JUN-1998;   98US-0087607.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Baker K,  Chen J,  Goddard A,  Gurney AL,  Smith V,  Watanabe CK;
PI   Wood WI,  Yuan J;
XX
DR   WPI; 2000-072883/06.
DR   N-PSDB; AAZ65071.
XX
PT   Membrane-bound proteins and related nucleotide sequences  -
XX
PS   claim 12; Fig 228; 822pp; English.
XX
CC   The invention provides membrane-bound PRO polypeptides and
CC   polynucleotides encoding them. The PRO sequences of the invention were
CC   identified based on extracellular domain homology screening. The PRO
CC   sequences have homology with proteins including LDL receptors, TIE
CC   ligands and various enzymes. The membrane-bound proteins and receptor
CC   molecules are useful as pharmaceutical and diagnostic agents. Receptor
CC   immunoadhesins, for instance, can be used as therapeutic agents to block
CC   receptor-ligand interactions. The membrane-bound proteins can also be
CC   employed for screening of potential peptide or small molecule inhibitors
CC   of the relevant receptor/ligand interaction. The PRO encoding sequences
CC   are useful as hybridization probes, in chromosome and gene mapping and in
CC   the generation of antisense RNA and DNA. PRO nucleic acid sequences
CC   will also be useful for the preparation of PRO polypeptides, especially
CC   by recombinant techniques.
XX
SQ   Sequence   461 AA;

  Query Match             100.0%;  Score 2450;  DB 21;  Length 461;
  Best Local Similarity   100.0%;  Pred. No. 5.5e-225;
  Matches  461;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MVNDRWKTMGGAAQLEDRPRDKPQRPSCGYVLCTVLLALAVLLAVAVTGAVLFLNHAHAP 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MVNDRWKTMGGAAQLEDRPRDKPQRPSCGYVLCTVLLALAVLLAVAVTGAVLFLNHAHAP 60

Qy         61 GTAPPPVVSTGAASANSALVTVERADSSHLSILIDPRCPDLTDSFARLESAQASVLQALT 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GTAPPPVVSTGAASANSALVTVERADSSHLSILIDPRCPDLTDSFARLESAQASVLQALT 120

Qy        121 EHQAQPRLVGDQEQELLDTLADQLPRLLARASELQTECMGLRKGHGTLGQGLSALQSEQG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 EHQAQPRLVGDQEQELLDTLADQLPRLLARASELQTECMGLRKGHGTLGQGLSALQSEQG 180
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A cont'd

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Qy        181 RLIQLLSESQGHMAHLVNSVSDILDALQRDRGLGRPRNKADLQRAPARGTRPRGCATGSR 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 RLIQLLSESQGHMAHLVNSVSDILDALQRDRGLGRPRNKADLQRAPARGTRPRGCATGSR 240

Qy        241 PRDCLDVLLSGQQDDGVYSVFPTHYPAGFQVYCDMRTDGGGWTVFQRREDGSVNFFRGWD 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 PRDCLDVLLSGQQDDGVYSVFPTHYPAGFQVYCDMRTDGGGWTVFQRREDGSVNFFRGWD 300

Qy        301 AYRDGFGRLTGEHWLGLKRIHALTTQAAYELHVDLEDFENGTAYARYGSFGVGLFSVDPE 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 AYRDGFGRLTGEHWLGLKRIHALTTQAAYELHVDLEDFENGTAYARYGSFGVGLFSVDPE 360

Qy        361 EDGYPLTVADYSGTAGDSLLKHSGMRFTTKDRDSDHSENNCAAFYRGAWWYRNCHTSNLN 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 EDGYPLTVADYSGTAGDSLLKHSGMRFTTKDRDSDHSENNCAAFYRGAWWYRNCHTSNLN 420

Qy        421 GQYLRGAHASYADGVEWSSWTGWQYSLKFSEMKIRPVREDR 461
              |||||||||||||||||||||||||||||||||||||||||
Db        421 GQYLRGAHASYADGVEWSSWTGWQYSLKFSEMKIRPVREDR 461
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Sequence Comparison B

```
ID   AAB19732 standard; Protein; 269 AA.
XX
AC   AAB19732;
XX
DT   19-FEB-2001  (first entry)
XX
DE   Human SECX Clone 4437909.0.4 encoded protein.
XX
KW   SECX; human; diagnosis; therapy; reproductive disorder;
KW   muscular disorder; immunological disorder; cancer; infection.
XX
OS   Homo sapiens.
XX
PN   WO200061754-A2.
XX
PD   19-OCT-2000.
XX
PF   07-APR-2000; 2000WO-US09392.
XX
PR   09-APR-1999;   99US-0128514.
PR   03-MAR-2000; 2000US-0128514.
XX
PA   (CURA-) CURAGEN CORP.
XX
PI   Fernandez E,  Vernet C,  Shimkets R;
XX
DR   WPI; 2000-679487/66.
DR   N-PSDB; AAA88801.
XX
PT   SECX polypeptides and the nucleic acids that encode them, useful for
PT   diagnosing, preventing and treating e.g. cancers, inflammation,
PT   arthritis and immunological disorders -
XX
PS   Claim 1; Fig 13; 143pp; English.
XX
CC   The present sequence is that of the protein encoded by novel SECX
CC   Clone 4437909.0.4 (see AAA88801).  It is a microbody (peroxisome)
CC   associated protein expressed in osteogenic sarcoma cell lines,
CC   adrenal gland, thalamus, foetal brain and foetal lung.  The
CC   invention provides novel SECX polynucleotides (see AAA88789-804) and
CC   the secreted or membrane-associated proteins encoded by them (see
CC   AAB19720-34).  SECX polynucleotides, polypeptides and antibodies can
CC   be used in the detection, diagnosis and treatment (including gene
CC   therapy) of a broad range of pathological states.  4437909.0.4
CC   protein shows similarity to human microfibril-associated glycoprotein
CC   4 splice variant MAG4V and may therefore be useful for treating
CC   reproductive disorders (e.g. disruptions of the oestrus cycle and
CC   spermatogenesis, polycystic ovary syndrome and cancers of the
CC   prostate and ovary), muscular disorders (e.g. Duchenne's muscular
CC   dystrophy, lipid myopathy and myocarditis), immunological
CC   disorders (e.g. Addison's disease, asthma, anaemia and AIDS) and
CC   neoplastic disorders (e.g. myeloma, sarcoma, leukaemia and lung
CC   cancer).  Similarity is also shown to human opsonin protein P35,
CC   suggesting use in the prevention and treatment of infectious
CC   diseases.  A variant of 4437909.0.4 is given in AAB19733.
XX
SQ   Sequence   269 AA;
```

```
  Query Match             60.5%;  Score 1483;  DB 21;  Length 269;
  Best Local Similarity   100.0%;  Pred. No. 6.1e-133;
  Matches  269;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy        193 MAHLVNSVSDILDALQRDRGLGRPRNKADLQRAPARGTRPRGCATGSRPRDCLDVLLSGQ 252
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MAHLVNSVSDILDALQRDRGLGRPRNKADLQRAPARGTRPRGCATGSRPRDCLDVLLSGQ 60

Qy        253 QDDGVYSVFPTHYPAGFQVYCDMRTDGGGWTVFQRREDGSVNFFRGWDAYRDGFGRLTGE 312
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 QDDGVYSVFPTHYPAGFQVYCDMRTDGGGWTVFQRREDGSVNFFRGWDAYRDGFGRLTGE 120

Qy        313 HWLGLKRIHALTTQAAYELHVDLEDFENGTAYARYGSFGVGLFSVDPEEDGYPLTVADYS 372
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 HWLGLKRIHALTTQAAYELHVDLEDFENGTAYARYGSFGVGLFSVDPEEDGYPLTVADYS 180

Qy        373 GTAGDSLLKHSGMRFTTKDRDSDHSENNCAAFYRGAWWYRNCHTSNLNGQYLRGAHASYA 432
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 GTAGDSLLKHSGMRFTTKDRDSDHSENNCAAFYRGAWWYRNCHTSNLNGQYLRGAHASYA 240

Qy        433 DGVEWSSWTGWQYSLKFSEMKIRPVREDR 461
              |||||||||||||||||||||||||||||
Db        241 DGVEWSSWTGWQYSLKFSEMKIRPVREDR 269
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Sequence Comparison C

```
MFA4_HUMAN
ID   MFA4_HUMAN     STANDARD;      PRT;   255 AA.
AC   P55083;
DT   01-OCT-1996 (Rel. 34, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Microfibril-associated glycoprotein 4 precursor.
GN   MFAP4.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Placenta;
RX   MEDLINE=95359962; PubMed=7633408;
RA   Zhao Z., Lee C.-C., Jiralerspong S., Juyal R.C., Lu F., Baldini A.,
RA   Greenberg F., Caskey C.T., Patel P.I.;
RT   "The gene for a human microfibril-associated glycoprotein is commonly
RT   deleted in Smith-Magenis syndrome patients.";
RL   Hum. Mol. Genet. 4:589-597(1995).
CC   -!- FUNCTION: COULD BE INVOLVED IN CALCIUM-DEPENDENT CELL ADHESION OR
CC       INTERCELLULAR INTERACTIONS.
CC   -!- SUBCELLULAR LOCATION: Secreted; extracellular matrix.
CC   -!- SIMILARITY: Contains 1 fibrinogen C-terminal domain.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; L38486; AAB00968.1; ALT_INIT.
DR   HSSP; P02671; 1FZD.
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DR   Genew; HGNC:7035; MFAP4.
DR   MIM; 600596; -.
DR   GO; GO:0001527; C:microfibril; NAS.
DR   GO; GO:0007155; P:cell adhesion; NAS.
DR   InterPro; IPR002181; Fibrinogen_C.
DR   Pfam; PF00147; fibrinogen_C; 1.
DR   SMART; SM00186; FBG; 1.
DR   PROSITE; PS00514; FIBRIN_AG_C_DOMAIN; FALSE_NEG.
KW   Cell adhesion; Extracellular matrix; Glycoprotein; Calcium;
KW   Signal.
FT   SIGNAL        1     20       POTENTIAL.
FT   CHAIN        21    255       MICROFIBRIL-ASSOCIATED GLYCOPROTEIN 4.
FT   DOMAIN       57    255       FIBRINOGEN C-TERMINAL.
FT   SITE         26     28       CELL ATTACHMENT SITE (POTENTIAL).
FT   CARBOHYD     87     87       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    137    137       N-LINKED (GLCNAC. . .) (POTENTIAL).
SQ   SEQUENCE   255 AA;  28648 MW;  B8F0B47AC694435E CRC64;

  Query Match             27.0%;  Score 662.5;  DB 1;  Length 255;
  Best Local Similarity   55.8%;  Pred. No. 4e-42;
  Matches  121;  Conservative   32;  Mismatches   63;  Indels    1;  Gaps    1;

Qy        240 RPRDCLDVLLSGQQDDGVYSVFPTHYPAGFQVYCDMRTDGGGWTVFQRREDGSVNFFRGW 299
              :| || |:   | | |||| ::|:       |:||| |:|| |||||:| :|||:|||||
Db         37 QPLDCDDIYAQGYQSDGVYLIYPSGPSVPVPVFCDMTTEGGKWTVFQKRFNGSVSFFRGW 96

Qy        300 DAYRDGFGRLTGEHWLGLKRIHALTTQAAYELHVDLEDFENGTAYARYGSFGVGLFSVDP 359
              : |: ||||  ||:||||: :| || :  ||| |||||||| ||||:|  | :   :|
Db         97 NDYKLGFGRADGEYWLGLQNMHLLTLKQKYELRVDLEDFENNTAYAKYADFSISPNAVSA 156

Qy        360 EEDGYPLTVADY-SGTAGDSLLKHSGMRFTTKDRDSDHSENNCAAFYRGAWWYRNCHTSN 418
              ||||| | || :  | |||||  ||| :|:| ||| |    ||||   ||:|:|:|| :|
Db        157 EEDGYTLFVAGFEDGGAGDSLSYHSGQKFSTFDRDQDLFVQNCAALSSGAFWFRSCHFAN 216

Qy        419 LNGQYLRGAHASYADGVEWSSWTGWQYSLKFSEMKIR 455
              ||| || |:| |||:|: |: | |: |||| :|||||
Db        217 LNGFYLGGSHLSYANGINWAQWKGFYYSLKRTEMKIR 253
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